Involuntary Smoking and Asthma Severity in Children*

Data From the Third National Health and Nutrition Examination Survey

Raymond had

David M. Mannino, MD, FCCP; David M. Homa, PhD; and Stephen C. Redd, MD

Study objectives: **We sought to determine the indicators of asthma severity among children in the United States with high and low levels of tobacco smoke exposure.**
Design: **Cross-sectional study.**
Setting: **Nationally representative survey of participants in the Third National Health and Nutrition Examination Survey (from 1988 to 1994).**
Participants: **Five hundred twenty-three children with physician-diagnosed asthma.**
Measurements and results: **We stratified the study participants into tertiles on the basis of serum levels of cotinine (a metabolite of nicotine that indicates tobacco smoke exposure). We used logistic and linear regression modeling, adjusting for known covariates, to determine the effect of high environmental tobacco smoke exposure on the following outcomes: asthma severity (determined using reported symptom and respiratory illness frequency); lung function; physician visits; and school absence. Among our study sample, 78.6% of children had mild asthma, 6.8% of children had moderate asthma, and 14.6% of children had severe asthma. Asthmatic children with high levels of smoke exposure, compared with those with low levels of exposure, were more likely to have moderate or severe asthma (odds ratio, 2.7 95% confidence interval [CI], 1.1 to 6.8) and decreased lung function, with a mean FEV_1 decrement of 213 mL or 8.1% (95% CI, −14.7 to −3.5).**
Conclusions: **Involuntary smoke exposure is associated with increased asthma severity and worsened lung function in a nationally representative group of US children with asthma.**
(CHEST 2002; 122:409–415)

Key words: asthma; children; tobacco smoke pollution

Abbreviations: CI = confidence interval; ETS = environmental tobacco smoke; MMEF = maximal midexpiratory flow; NHANES III = Third National Health and Nutrition Examination Survey; OR = odds ratio; SES = socioeconomic status

Involuntary smoking by children has been linked to respiratory infections, middle ear disease, and asthma.[1,2] Because asthma is associated with increased bronchial reactivity, children with asthma are vulnerable to air pollutants that originate from indoor, as well as outdoor, sources.[3–5] Many studies[6–8] that have examined the health effects of tobacco smoke on children have used reported smoke exposure or the presence of smokers in the child's household to define exposure. A limitation of these studies is that most children in the United States are exposed to tobacco smoke,[9] thus children in the "unexposed" category in these studies can have exposures from nonparental sources or in places other than the home. This becomes increasingly important as children get older and spend an increasing amount of time outside the home. A second limitation is that parents of children with respiratory disease may under-report the child's exposure to tobacco smoke.[10] Use of the biomarker cotinine, which is a metabolite of nicotine and a sensitive

For editorial comment see page 394

*From the Air Pollution and Respiratory Health Branch, Division of Environmental Hazards and Health Effects, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA.
This study was funded by the Centers for Disease Control and Prevention.
Manuscript received July 23, 2001; revision accepted February 5, 2002.
Correspondence to: David M. Mannino, MD, FCCP, National Center for Environmental Health, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS E-17, Atlanta, GA 30333; e-mail: dmannino@cdc.gov

indicator of tobacco smoke exposure, potentially can reduce misclassification, allowing comparison of a high-exposure group with a low-exposure group.[11]

We analyzed data, among children aged 4 through 16 years, from the Third National Health and Nutrition Examination Survey (NHANES III). In a prior analysis of this data set, we determined that among all surveyed children those with environmental tobacco smoke (ETS) exposure were more likely to have increased respiratory symptoms, increased school absences, and decreased lung function.[12] The present analysis was limited to children with a physician diagnosis of asthma, and we used serum cotinine levels as the basis for classifying children into ETS exposure groups to determine the indicators of asthma severity among children in the United States with high and low levels of tobacco smoke exposure.

Materials and Methods

Study Population

The National Center for Health Statistics of the Centers for Disease Control and Prevention (Atlanta, GA) conducted NHANES III.[13] NHANES III was approved by the Institutional Review Board of the National Center for Health Statistics, and the appropriate informed consent was obtained from survey participants. In this survey, a stratified, multistage, clustered probability design was used to select a representative sample of the civilian, noninstitutionalized US population. Survey participants completed extensive questionnaires and underwent comprehensive physical examinations, including pulmonary function testing, at a specially equipped mobile examination center. A knowledgeable proxy, usually a parent or guardian, completed questionnaires for participants who were < 17 years of age. Children ≥ 12 years of age self-reported tobacco use.

Participants and Demographics

We limited the analysis to children aged 4 to16 years for whom serum cotinine levels were available and who had a physician diagnosis of asthma. NHANES III participants underwent physical examinations that included pulmonary function testing for children aged ≥ 8 years of age. We excluded children who either reported current smoking or had cotinine levels of > 20 ng/mL, indicating possible current use of cigarettes or spit tobacco.[9]

Variable Definition

Respondents were asked "Has a doctor ever told you that your child has asthma?," and we restricted the analysis to those with a positive response. We classified the race of the participating children as either white or nonwhite, with the latter category including black children, Asian children, and children of other races. We classified socioeconomic status (SES) as "low" if the reference adult in the family (*ie*, one of the persons who owns the home or pays the rent) had a 12th grade education or less or the poverty index for the family was less than 1.[13] This index is determined on the basis of the family income and the number of people in the household. Family size was classified as five or more persons or four or fewer persons. If either the father or mother of the child was reported to have had asthma or hay fever at any age, the child was classified as having a parental history of allergy or asthma. For most analyses, we stratified participants into the following three age strata: 4 to 6 years; 7 to 11 years; and 12 to 16 years. The respondent was asked to classify the child's health status as excellent, very good, good, fair, or poor. We then classified children as having a less than very good health status compared with a very good or excellent health status.

Asthma Severity

We classified asthma severity based on the frequency of symptoms and respiratory illnesses. If the symptoms of cough or wheeze or the respiratory illnesses of sinusitis or upper respiratory illness were reported as having occurred for ≥ 12 days in the previous year, the child was classified as having moderate asthma. If these symptoms or illnesses were reported for > 300 days in the previous year (typically, those reporting daily symptoms), the child was classified as having severe asthma. We also classified children by the number of hospitalizations or physician visits for asthma that they had reported in the 12 months before the survey. Respondents were asked to list any prescription medications the children were using and the reasons for using these medications. We searched for medication that was being used for asthma and classified these as inhaled steroids, inhaled bronchodilators, or other medication.

Pulmonary Function Data

Spirometry was conducted on survey participants ≥ 8 years of age using a dry rolling seal spirometer in the mobile examination center. The procedures for testing were based on the 1987 American Thoracic Society recommendations.[14] To obtain spirometry results that were acceptable according to the protocol, five to eight forced expirations were performed. Several measures of lung function were used as follows: FEV_1; FVC; maximal midexpiratory flow (MMEF; determined by calculating the mean flow per second from 25% to 75% of the lung volume); and FEV_1/FVC ratio. Published prediction equations based on NHANES III data[15] were used to determine which participants had a low FEV_1, which was defined as $< 80\%$ of the predicted value.

Cotinine Levels

Serum cotinine levels were determined using high-performance liquid chromatography, atmospheric-pressure chemical ionization, and tandem mass spectrometry, as has been described elsewhere.[9] We stratified the children into tertiles, based on cotinine levels of 0.050 ng/mL (the limit of detection; children with no detectable cotinine were included in this tertile) to 0.115 ng/mL (low level), 0.116 to 0.639 ng/mL (intermediate level), and 0.640 to 20 ng/mL (high level).

Statistical Analysis

We calculated all estimates using the appropriate sampling weight to represent US children aged 4 to 16 years. The purpose of the sampling weight is to provide population estimates that adjust for unequal probabilities of selection and account for nonresponse. The weights were poststratified to the US population as estimated by the Bureau of the Census. For analyses, we used two software packages (SAS, version 6; SAS Institute; Cary, NC; and SUDAAN, version 7; Research Triangle Institute; Research Triangle Park, NC [a program that adjusts for complex

sample design when variance estimates are calculated]).[16,17] Using logistic regression, we modeled factors predicting asthma severity, physician visits for asthma, hospitalizations for asthma, and FEV_1 < 80% predicted, adjusting for age, for race/ethnicity, SES, family size, and parental history of asthma. Each model was evaluated for evidence of effect modification and confounding. For the evaluation of continuous lung function data (*ie*, FEV_1, FEV_1/FVC ratio, FVC, and MMEF), we developed linear regression models that adjusted for age, sitting height, sex, race/ethnicity, SES, parental history of allergy or asthma, family size, and cotinine levels. In addition, we used χ^2 tests of trends in proportions (Epi-Info, version 6.04; Centers for Disease Control and Prevention; Atlanta, GA) to determine whether trends for asthma hospitalizations, physician visits, health status, FEV_1 < 80% predicted, use of inhaled bronchodilators, and use of inhaled corticosteroids were significant across strata of increasing asthma severity and tobacco smoke exposure.

Results

Of the 13,944 children aged 2 months through 16 years who participated in NHANES III, 1,025 had physician-diagnosed asthma. Of this group, we excluded 308 who were < 4 years old, 36 who had not had a physical examination, 145 who had not had cotinine levels determined (typically because the blood sample was not enough for the cotinine analysis), and 13 who had cotinine levels of > 20 ng/mL, suggesting current smoking or spit tobacco use, resulting in 523 children in our analytic sample. Of these children, 294 completed pulmonary function testing.

The 523 children in our final sample represented approximately 4.3 million US children. Their demographic characteristics are depicted in Table 1. Our analysis of asthma severity resulted in the classification of 78.6% of the children as having mild asthma, 6.8% of the children as having moderate asthma, and 14.6% of the children as having severe asthma (Table 2). Other indicators of asthma severity, including any hospitalization for asthma in the prior year, any physician visit for asthma in the prior year, a less than very good health status, and the mean number of school absence days also were increased in children with more severe asthma (Table 2). Similarly, lung function was lower, and the use of inhaled bronchodilators or inhaled corticosteroids was higher in children with more severe asthma (Table 2).

Cotinine exposures varied by demographic subgroup, with a higher proportion of younger children, nonwhite children, lower SES children, and children who did not have a parent with asthma in the highest cotinine tertile (Table 3). Most indicators of asthma severity were higher among children with the highest smoke exposure. The only exception was for any hospitalization for asthma in the prior year, which was higher among children with the lowest smoke exposure. Lung function, as determined both by the proportion of children with an FEV_1 < 80% of predicted and by the mean FEV_1 as a percentage of the predicted value, was lower among children with high levels of smoke exposure. The use of inhaled bronchodilators was similar in the three exposure categories, whereas the use of inhaled corticosteroids was lower among children with the lowest smoke exposure, but this difference was not significant (Table 3).

Children with high levels of smoke exposure, compared with those with low levels of smoke exposure, were more likely to have had moderate or severe asthma (odds ratio [OR], 2.7; 95% confidence interval [CI], 1.1 to 6.8) after adjusting for covariates (Table 4). ORs ranged from 1.8 to 5.1 for outcomes of severe asthma, any physician visit for asthma in the prior year, an FEV_1 < 80% of predicted, and six or more days of absence from school in the prior year, although in all of these instances the CIs included 1 and were not statistically significant (Table 4). Children with high current smoke exposure were less likely to have reported a hospitalization for asthma in the previous year (Table 4). Children with moderate levels of smoke exposure, compared with those with low levels of smoke exposure, had ORs for the noted outcomes that were similar to those noted for children with high levels of exposure, although all of the CIs included 1 and were not statistically significant (data not shown).

Lung function, as indicated by the FEV_1, FVC, and MMEF, was significantly decreased by 8.1%

Table 1—*Covariates of Age, Sex, Race, SES, Asthma or Allergy in a Parent, and Family Size

Covariates	Weighted Population	Weighted %
Age group		
4–6 yr (n = 145)	680,000	15.9
7–11 yr (n = 202)	1,780,000	41.6
12–16 yr (n = 176)	1,820,000	42.6
Sex		
Male (n = 308)	2,530,000	59.2
Female (n = 215)	1,750,000	40.2
Race		
White (n = 381)	2,840,000	66.3
Nonwhite (n = 142)	1,440,000	33.7
SES		
Low (n = 382)	2,490,000	58.3
High (n = 141)	1,790,000	41.7
Parental asthma		
Yes (n = 204)	2,010,000	47.0
No (n = 319)	2,270,000	53.0
Family size		
≥ 6 persons (n = 259)	1,920,000	44.8
≤ 5 persons (n = 264)	2,360,000	55.2
Total (n = 523)	4,280,000	

*Data are from the NHANES III.[13]

Table 2—*Covariates for the Study Stratified by Asthma Severity**

Covariates	Asthma			p Value†
	Mild (n = 395)	Moderate (n = 39)	Severe (n = 89)	
Age group				
4–6 yr	15.0	22.6	17.2	0.509
7–11 yr	41.3	32.9	47.2	0.419
12–16 yr	43.7	44.5	35.6	0.043
Sex				
Male	61.0	36.9	60.0	0.365
Female	39.0	63.1	40.0	
Race				
White	67.5	77.7	54.7	0.059
Nonwhite	32.5	22.3	45.3	
SES				
Low	57.6	50.8	65.4	0.294
High	42.4	49.2	34.6	
Parental asthma				
Yes	45.2	61.5	49.6	0.275
No	54.8	38.5	50.4	
Family size				
≥ 5 persons	47.8	31.1	35.0	0.010
≤ 4 persons	52.2	68.9	65.0	
Outcomes				
Any hospitalization for asthma in prior year	4.4	6.7	12.3	0.003
Any physician visit for asthma in prior year	34.9	51.5	69.8	< 0.001
Less than very good health status	38.5	51.4	67.7	< 0.001
Mean school absences in prior year, d	6.9	14.2	9.6	< 0.001
Proportion with FEV_1 < 80% predicted	5.7	15.5	34.2	< 0.001
Mean FEV_1 as % predicted	96.8	92.0	90.5	< 0.001
Proportion using inhaled bronchodilators	21.7	31.0	62.8	< 0.001
Proportion using inhaled corticosteroids	1.1	5.9	24.0	< 0.001

*Values given as %, unless otherwise indicated. Data are from NHANES III.[13]
†χ^2 test of trend or *t* test comparing patients with mild asthma to those with severe asthma.

(95% CI, 3.5 to 14.7%), 5.6% (95% CI, 0.6 to 10.6%), and 12.5% (95% CI, 2.0 to 23.0%), respectively, in children with high levels of smoke exposure compared with those children with low levels of exposure (Table 5). This corresponds to a mean decrement of 213 mL for FEV_1, 179 mL for FVC, and 328 mL for MMEF. Children with intermediate levels of smoke exposure had lung function levels that were similar to the children with low smoke exposure (data not shown).

Discussion

Our primary findings are that children in whom asthma has been diagnosed by a physician have increased severity associated with tobacco smoke exposure. These children were significantly more likely to have more severe asthma, as indicated by increased symptoms of cough and wheeze, by an increased number of respiratory illnesses, and by lower levels of lung function. They were also more likely to have visited a physician more than once in the previous year, although this increase was not statistically significant. A surprising finding was that children with recent tobacco smoke exposure were less likely to have been hospitalized for asthma in the previous year.

Asthma prevalence, morbidity, and mortality have increased in the United States since 1980.[18] However, increases in asthma morbidity (as measured by hospitalizations, emergency department visits, and physician office visits) and asthma mortality have been generally proportional to the increase in asthma prevalence. Asthma surveillance has not included measures of symptom-defined severity; thus, whether asthma severity has changed over the past 2 decades is unknown. Asthma severity has been measured in individuals using both historical data and biological measurements, such a methacholine responsiveness or pulmonary function.[19] Guidelines from the National Asthma Education and Prevention Program include using historical data on symptoms (prior to any treatment) to classify patients into mild, moderate, and severe disease and intermittent disease.[19] Our estimate of the incidence of

Table 3—*Covariates for the Study Stratified by Cotinine Tertile

Covariates	Cotinine Level† High 0.64–20 ng/mL (n = 205)	Intermediate 0.116–0.639 ng/mL (n = 171)	Low < 0.116 ng/mL (n = 147)	p Value‡
Age group				
4–6 yr	31.1	8.0	8.8	< 0.001
7–11 yr	25.6	54.3	44.5	< 0.001
12–16 yr	43.3	37.7	46.7	0.6
Sex				
Male	61.2	59.4	57.1	0.476
Female	38.8	40.6	42.9	
Race				
White	62.8	61.9	74.0	0.225
Nonwhite	37.2	38.1	26.0	
SES				
Low	69.4	51.8	53.8	0.002
High	30.6	48.2	46.2	
Parental asthma				
Yes	43.4	41.9	55.3	0.042
No	56.6	58.1	44.7	
Family size				
≥ 5	46.7	48.3	39.5	0.206
≤ 4	53.3	51.7	60.5	
Outcomes				
Moderate or severe asthma	26.9	24.7	13.0	0.003
Severe asthma	15.8	18.9	9.4	0.158
Any hospitalization for asthma in prior year	2.8	3.4	10.9	< 0.001
Any physician visit for asthma in prior year	49.2	41.0	33.6	0.003
Less than very good health status	49.1	42.2	39.9	0.101
Mean school absences in prior year, d	8.7	8.1	6.6	< 0.001
Proportion with FEV_1 < 80% of predicted†	18.4	10.7	4.0	< 0.001
Mean FEV_1 as % of predicted†	92.3	95.0	98.4	< 0.001
Proportion using inhaled bronchodilators	27.0	27.4	30.4	0.451
Proportion using inhaled corticosteroids	3.3	9.7	1.4	0.601

*Values given as %, unless otherwise indicated. Data are from NHANES III.[13]
†High = 0.64 to 20 ng/mL; intermediate = 0.116 to 0.639 ng/mL; low = < 0.116 ng/mL.
‡χ^2 test of trend or *t* test comparing high to low cotinine levels.

moderate or severe asthma (21.4%) is lower than another national estimate of asthma severity in children (38.4%)[20] and is much lower than the estimate in an inner city study of asthma (62%).[21]

The use of symptoms to classify severity may be more accurate than the use of medication or outcomes, particularly in this database for which only 4% of the children with asthma were receiving therapy with inhaled steroids and 25% reported inhaled β-agonist use.[6,22] Even the use of symptoms, though, may not necessarily reflect the true severity of the asthma as assessed by a specialist.[23]

Table 4—*Comparing Children With the Highest Cotinine Levels to Those With the Lowest Levels

Outcome	Proportion, %	Unadjusted OR	Unadjusted 95% CI	Adjusted OR	Adjusted 95% CI
Moderate or severe asthma	21.5	2.5	0.97–6.2	2.7	1.1–6.8
Severe asthma	14.6	1.8	0.6–5.7	1.9	0.6–5.7
Any physician visit for asthma in previous year	41.2	1.9	0.96–3.8	1.8	0.9–3.8
Any hospitalization for asthma in previous year	5.7	0.2	0.1–0.7	0.2	0.1–0.5
FEV_1 < 80% predicted	10.3	5.4	0.9–32.2	5.1	0.7–40.6
Less than very good health status	43.6	1.5	0.8–2.5	1.3	0.7–2.5
≥ 6 school absences in prior year	44.4	1.6	0.8–3.1	1.8	0.9–3.6

*Data are from NHANES III.[13]

Table 5—*Comparison of Children in Highest Cotinine Tertile to Those in Lowest Tertile on the Basis of Four Parameters

Parameter	Mean	Adjusted Model	
		Mean Effect, %	95% CI
FEV_1	2,633 mL	−8.1	−14.7–−3.5
FVC	3,199 mL	−5.6	−10.6–−0.6
FEV_1/FVC ratio	81.7%	−3.0	−6.5–0.5
MMEF	2,624 mL/s	−12.5	−23.0–−2.0

*Data are from NHANES III.[13]

Our finding that increased asthma severity was associated with high cotinine levels, which was based on increased symptoms of cough and or wheeze and number of reported respiratory illnesses, is an expected result. Many studies[24–26] have demonstrated that smoke exposure is deleterious for children with asthma, and clinic-based studies[5,27] also have used cotinine levels to determine worsened asthma severity in children who have experienced tobacco smoke exposure, although the present study is unique in that it is nationally representative and uses serum cotinine levels to document exposure. Decreased respiratory function among children with asthma, as indicated by lower levels of FEV_1 and a higher proportion of children with an FEV_1 levels of < 80% of the predicted value, which are associated with increased levels of cotinine, is also an expected finding[27–29] but has not been reported previously in a nationally representative population and has not been verified using serum cotinine levels. The decrement of 8.1% (a mean decrement of 213 mL) in the FEV_1 level among ETS-exposed children with asthma is more than four times greater than the corresponding decrement of 1.8% that we found in all children, suggesting that children with asthma are particularly susceptible to ETS.[12]

An unexpected finding was that asthma hospitalizations in the previous year were significantly decreased in children with the highest cotinine levels. The overall proportion of children reporting asthma hospitalizations in the previous year was 5.7%, which is higher than the proportion of 2 to 3% that one would expect from national surveillance data.[18] The survey design did not validate the parental reports of hospitalizations, thus, this outcome may have been misreported or overestimated. Another possibility, given that cotinine levels only measure several days of smoke exposure, is that some parents may have altered their home smoking policies in response to an asthma hospitalization. A final possibility is that tobacco smoke exposure in this age group increases symptoms but does not lead to serious consequences, such as hospitalization. Given that tobacco smoke exposure is associated with increased reporting of symptoms and lower lung function levels, this exposure is unlikely to protect against hospitalization for asthma.

The interpretation of these data are subject to several potential limitations. Cotinine, which has a half-life of 16 h, accurately measures recent, but not remote, exposure to ETS. The questionnaire data were not validated by reviews of medical records or physician interviews. Furthermore, physician diagnosis of asthma may not be consistent across the country. Although the NHANES III sample was large, the analysis may have lacked the power to detect small increases in the ORs for some of the outcomes. Moreover, children may change their behavior on the basis of symptoms. Children, particularly older ones or those with asthma, who are bothered by smoke may avoid it, resulting in lower cotinine levels. Because this is a cross-sectional study, one cannot conclude with certainty that tobacco smoke exposure caused the reported findings. It is possible that some of our findings are related either to residual confounding or to unmeasured confounders. Another potential bias is that the inclusion in our analyses of SES, which is consistently related to ETS exposure, may have resulted in an underestimate of some effects. Despite these potential limitations, most of our findings were consistent with what is reported in the literature.

In conclusion, this study provides evidence that children with asthma who are exposed to tobacco smoke have, generally, increased asthma severity and decreased lung function. Parents and caretakers of children with asthma need to be aware of this and need reduce or eliminate tobacco smoke exposure.

References

1 Cook DG, Strachan DP. Health effects of passive smoking-10: summary of effects of parental smoking on the respiratory health of children and implications for research. Thorax 1999; 54:357–366

2 Infante-Rivard C. Childhood asthma and indoor environmental risk factors. Am J Epidemiol 1993; 137:834–844

3 Evans D, Levison MJ, Feldman CH, et al. The impact of passive smoking on emergency room visits of urban children with asthma. Am Rev Respir Dis 1987; 135:567–572

4 Forastiere F, Corbo GM, Michelozzi P, et al. Effects of environment and passive smoking on the respiratory health of children. Int J Epidemiol 1992; 21:66–73

5 Oddoze C, Dubus JC, Badier M, et al. Urinary cotinine and exposure to parental smoking in a population of children with asthma. Clin Chem 1999; 45:505–509

6 Gergen PJ, Fowler JA, Maurer KR, et al. The burden of environmental tobacco smoke exposure on the respiratory health of children 2 months through 5 years of age in the United States: Third National Health and Nutrition Examination Survey, 1988 to 1994. Pediatrics 1998; 101:E8

7 Cunningham J, O'Connor GT, Dockery DW, et al. Environmental tobacco smoke, wheezing, and asthma in children in 24 communities. Am J Respir Crit Care Med 1996; 153:218–224
8 Fielder HM, Lyons RA, Heaven M, et al. Effect of environmental tobacco smoke on peak flow variability. Arch Dis Child 1999; 80:253–256
9 Pirkle JL, Flegal KM, Bernert JT, et al. Exposure of the US population to environmental tobacco smoke: the Third National Health and Nutrition Examination Survey, 1988 to 1991. JAMA 1996; 275:1233–1240
10 Kohler E, Sollich V, Schuster R, et al. Passive smoke exposure in infants and children with respiratory tract diseases. Hum Exp Toxicol 1999; 18:212–217
11 Benowitz NL. Cotinine as a biomarker of environmental tobacco smoke exposure. Epidemiol Rev 1996; 18:188–204
12 Mannino DM, Moorman JE, Kingsley B, et al. Health effects related to environmental tobacco smoke exposure in children in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Pediatr Adolesc Med 2001; 155:36–41
13 National Center for Health Statistics. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988–1994; series 1—programs and collection procedures. Vital Health Stat 1 1994; 1–407
14 Standardization of spirometry: 1987 update; statement of the American Thoracic Society. Am Rev Respir Dis 1987; 136: 1285–1298
15 Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999; 159:179–187
16 Shah BV, Barnwell BG, Bieler GS. SUDAAN user's manual, release 7.0. Research Triangle Park, NC: Research Triangle Institute, 1996
17 SAS Institute. SAS, version 6. Cary, NC: SAS Institute, 1990
18 Mannino DM, Homa DM, Pertowski CA, et al. Surveillance for asthma: United States, 1960–1995. MMWR Morb Mortal Wkly Rep 1998; 47:1–27
19 Sheffer AL, Taggart VS. The National Asthma Education Program: expert panel report guidelines for the diagnosis and management of asthma; National Heart, Lung, and Blood Institute. Med Care 1993; 31(suppl):MS20–MS28
20 Schulman R. Bucuvalas Research Asthma in America. Available at: http://www.asthmainamerica.com/. Accessed July 12, 2002
21 Eggleston PA, Malveaux FJ, Butz AM, et al. Medications used by children with asthma living in the inner city. Pediatrics 1998; 101:349–354
22 Halterman JS, Aligne CA, Auinger P, et al. Inadequate therapy for asthma among children in the United States. Pediatrics 2000; 105:272–276
23 Osborne ML, Vollmer WM, Pedula KL, et al. Lack of correlation of symptoms with specialist-assessed long-term asthma severity. Chest 1999; 115:85–91
24 Abulhosn RS, Morray BH, Llewellyn CE, et al. Passive smoke exposure impairs recovery after hospitalization for acute asthma. Arch Pediatr Adolesc Med 1997; 151:135–139
25 Murray AB, Morrison BJ. Passive smoking and the seasonal difference of severity of asthma in children. Chest 1988; 94:701–708
26 Strachan DP, Cook DG. Health effects of passive smoking: 6. Parental smoking and childhood asthma: longitudinal and case-control studies. Thorax 1998; 53:204–212
27 Chilmonczyk BA, Salmun LM, Megathlin KN, et al. Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. N Engl J Med 1993; 328:1665–1669
28 Azizi BH, Henry RL. Effects of indoor air pollution on lung function of primary school children in Kuala Lumpur. Pediatr Pulmonol 1990; 9:24–29
29 Sherrill DL, Martinez FD, Lebowitz MD, et al. Longitudinal effects of passive smoking on pulmonary function in New Zealand children. Am Rev Respir Dis 1992; 145: 1136–1141